

Effects of Ionizing Radiation Exposure

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Brief History of Ionizing Radiation

Historical Perspective of Radiation

1895 – first observance of ionizing radiation (x-rays) by Wilhelm Roentgen

1896 – use of x-rays for medical diagnostics proposed by

Roentgen

1898 – beneficial, or hormetic, effects of low doses of x-rays observed

1902 – effectiveness of “radium rays” (gamma-rays) for treating skin cancer recognized



Historical Perspective (cont.)

1904 – first death from excessive x-ray exposure recorded (about 100 deaths occurred from afflictions possibly related to ionizing radiation exposure by 1922)

1898 to 1970 – physicians used x-rays and radium to

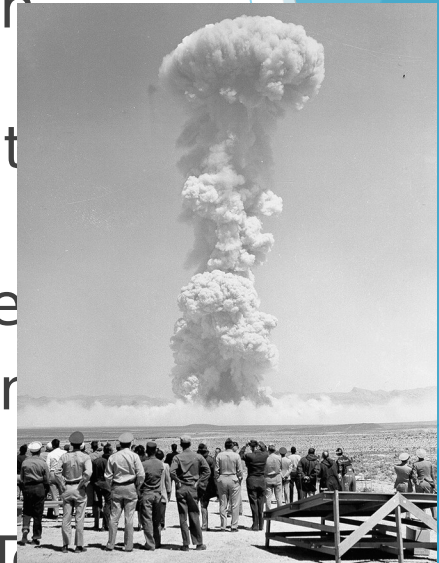
- ▶ heal wounds faster
- ▶ stop infections (gas gangrene, boils, sinus, inner ear, whooping cough, pneumonia, etc.)
- ▶ relieve arthritis and other inflammatory conditions
- ▶ treat asthma, autoimmune diseases, type 1 diabetes

(No reported evidence of increased cancer in patients subjected to such radiation treatments^{a,b})

Historical Perspective (cont.)

Abrupt change in public mood regarding radiation after WW II due to political and social issues related to nuclear weapon testing

- ▶ Claims of long-term adverse health effects from low dose radioactive fallout originally used in attempts to halt nuclear weapon testing
- ▶ Claims of adverse radiation-induced health effects from fallout still being alleged today despite termination of above-ground testing by Limited Test Ban Treaty of 1963 and no proven adverse health effects



Living with Low-Dose Ionizing Radiation

Important Note Regarding Chronic Low-Dose Radiation Exposure

Chronic low-dose radiation exposure from natural background radiation generally expressed as annual dose

- ▶ Implies biological cell damage from chronic exposure to low-dose/dose-rate radiation is cumulative, ignoring body's adaptive protection responses
- ▶ Such exposure more appropriately expressed as hourly or daily dose, since radiation-induced cell damage repaired in about 24 hours
- ▶ Chronic dose-rate from natural background radiation not high enough to result in adverse health effects

Natural Background Radiation

- ▶ Natural background radiation sources shown below result in chronic exposures that vary around the world
- ▶ External sources of high energy electromagnetic radiation include cosmic rays from beyond Earth and gamma-rays from radioactive decay of uranium and thorium in Earth's crust

US Average -- 340 nSv/h

Cosmic	34 nSv/h
Terrestrial	34 nSv/h
Internal (K-40)	45 nSv/h
Inhaled (Radon)	227 nSv/h

Internal Radionuclides

- ▶ Potassium and carbon, essential elements that make up human body, contain radioactive K-40 and C-14 (both β emitters), respectively
- ▶ Majority of internal radiation exposure from K-40

US Average -- 340 nSv/h

Cosmic	34 nSv/h
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Internal (K-40)	45 nSv/h
Inhaled (Radon)	227 nSv/h

Exposure from Inhaled Radon

- ▶ Radon gas in air we breathe comes from radioactive decay of uranium and thorium in Earth's crust (varies around the world)
- ▶ Inhaled radon (α emitter) is largest contributor to natural background radiation exposure

US Average -- 340 nSv/h

Cosmic	34
nSv/h	

Terrestrial	34
nSv/h	

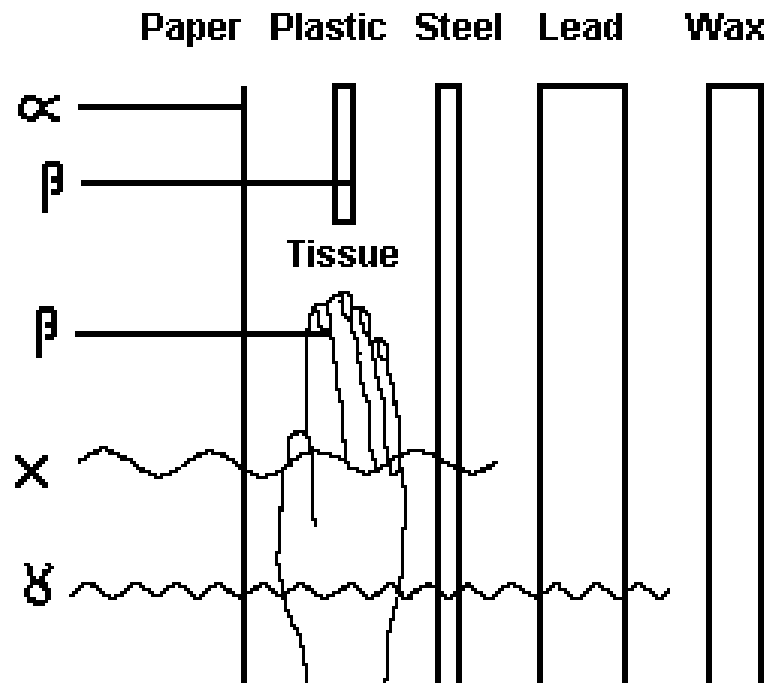
Internal (K-40)	45
nSv/h	

Inhaled (Radon)	227
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Penetrating Properties of Ionizing Radiation

Alpha and beta particles can't penetrate dead layer of human skin; only health concern as internal source of radiation

Gamma-rays and x-rays penetrate human body; both external and internal radiation health concerns



Types of Radiation Exposure

- ▶ Acute Dose
 - Dose delivered over short period of time (e.g., chest x-ray)
 - Magnitude can be low or high, depending on dose-rate
 - **Not harmful at low dose-rate**
- ▶ Chronic Dose
 - Dose delivered over extended period of time (e.g., natural background radiation)
 - Low dose received at low dose-rate
 - **Not cumulative**; doesn't inhibit body's adaptive protection mechanisms that repair radiation-induced cell damage
- ▶ Dose Rate Effect
 - High dose-rates may overwhelm biological adaptive protection mechanisms; low dose-rates do not

External vs Internal Chronic Exposure

- ▶ Chronic external exposure to natural background radiation not health hazard (chronic dose not cumulative)
- ▶ Chronic internal exposures posing no health hazard
 - natural radioisotope body burdens (e.g., carbon-14 and potassium-40)
 - inhaled radon
 - medical diagnostic radioisotopes with short half-lives (e.g., iodine-131)
- ▶ Chronic internal exposures from unknowingly-ingested radioisotopes could be high enough to result in adverse health effects (e.g., radium dial painters)

Absorbed vs Equivalent Dose

- ▶ For low LET* radiation (i.e., beta particles and gamma-rays) absorbed dose (mGy) and equivalent dose (mSv) are same
 - Doses from low LET radiation applicable for both external and internal exposures
- ▶ For high LET radiation (i.e., alpha particles) equivalent dose is about 20 times absorbed dose (i.e., does more biological harm for same absorbed dose than low LET radiation)
 - Doses from high LET radiation applicable only for internal exposures as alpha particles have very limited range in air and cannot penetrate dead layer of human skin

* LET - linear energy transfer; expression of how quickly radiation energy
lost in radiation interactions

Internal Radionuclide Concerns

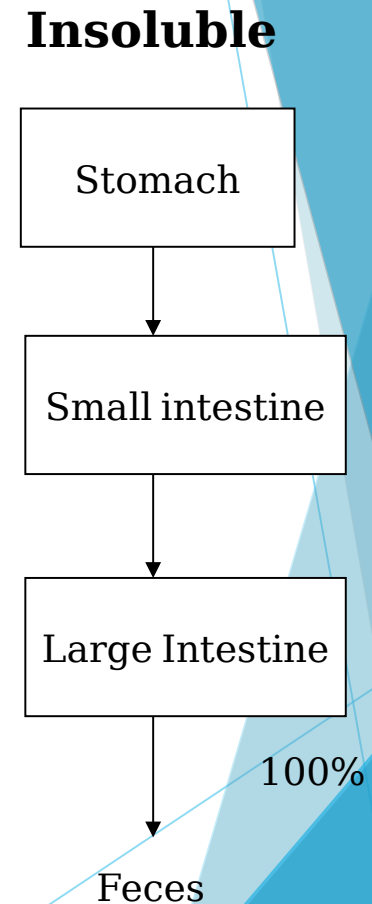
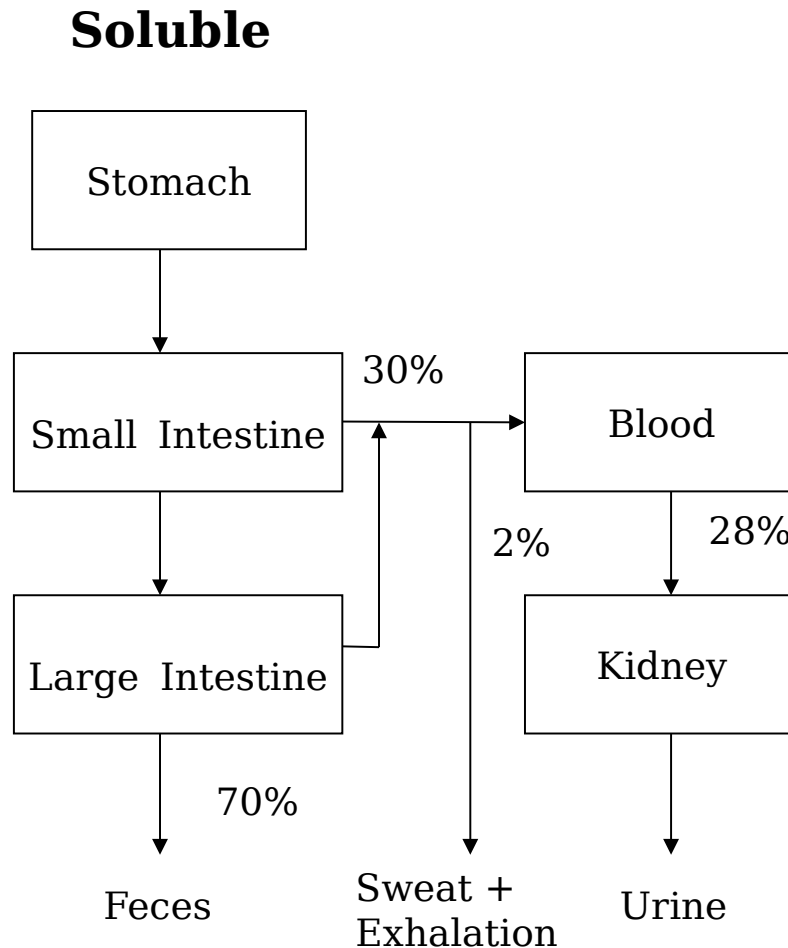
Ingestion of Radionuclides

- ▶ Ingestion most important route for introduction of radionuclides into organisms, giving rise to internal exposures
- ▶ Radioactive compounds generally considered insoluble if absorption through GI tract $<5\%$
- ▶ Soluble radioactive compounds show wide range of GI absorption percentages

GI Absorption of Radionuclides

Isotope	Radiation	Radiological Half-life	GI Absorption
Hydrogen-3 (Tritium)	β	12 years	100%
Strontium-89	β	51 days	30%
Strontium-90/Yttrium-90	β	29 years	30%
Zirconium-95/Niobium-95	β, γ	64 days	0.01%
Ruthenium-103	β, γ	39 days	0.03%
Ruthenium-106/Rhodium-106	β, γ	1 year	0.03%
Iodine-131	β, γ	8 days	100%
Cesium-137	β, γ	30 years	100%
Barium-140/Lanthanum-140	β, γ	13 days	5%
Cerium-141	β, γ	33 days	0.01%
Cerium-144/Praseodymium-144	β, γ	285 days	0.01%
Promethium-147	β	3 years	0.01%

Biological Excretion Pathways



Radionuclide Effective Half-life

- ▶ Radiological half-life – time it takes for one-half of radionuclide to decay to some other nuclide
- ▶ Biological half-life - time it takes for body to excrete one-half of material absorbed, ingested or inhaled
- ▶ Effective half-life – reduction of radioactive material in body by one-half through both radioactive decay and biological excretion
 - Calculated as sum of inverse radiological and biological half-lives

Half-Lives of Common Radionuclides in Human Body

<u>Radionuclides</u> <u>(Days)</u>	Radiological Half-Life (Days)	Biological Half-Life (Days)	Effective Half-Life (Days)
Hydrogen-3	4.5x10 ³	12	12
Carbon-14	2.1x10 ⁶	40	40
Phosphorus-32	14.3	1155	14.1
Sulfur-35	87.1	90	44.3
Chromium-51	27.8	616	26.6
Manganese-54	300	25	23.1
Iron-59	45.1	600	41.9
Cobalt-58	72	9.5	8.4
Cobalt-60	1.9x10 ³	9.5	9.5
Zinc-65	245	933	194
Rubidium-87	1.8x10 ¹³	60	60
Strontium-90	1.0x10 ⁴	1.8x10 ⁴	6.4x10 ³
Technetium-99m	0.25	1	0.21
Iodine-131	8	138	7.6
Cesium-134	840	70	64.6
Cesium-137	1.1x10 ⁴	70	70
Iridium-192	74.5	20	15.8
Gold-198	2.7	120	2.6
Mercury-203	45.8	14.5	11
Radon-222	3.83	None	3.83
Radium-226	5.9x10 ⁵	1.64x10 ⁴	1.6x10 ⁴
Uranium-235	2.6x10 ¹¹	300	300
Plutonium-239	8.9x10 ⁶	7.3x10 ⁴	7.2x10 ⁴

$$1/t_e = 1/t_r + 1/t_b$$

Critical Organs for Selected Radionuclides

Radioisotope

Critical Organ

Hydrogen-3 (Tritium)	Whole Body
Phosphorous-32	Bone
Carbon-14	Fat
Sulfur-35	Testes, Whole body
Chromium-51	Lower Intestine
Cobalt-60	Lower Large Intestine
Zinc-65	Liver, Prostate
Rubidium-87	Pancreas
Strontium-89, 90	Bone
Yttrium-91	Bone
Technetium-99m	Upper Large Intestine
Ruthenium-103, 106	Kidney
Iodine-125, 131 - 135	Thyroid
Tellurium-129m	Kidney
Cesium-137	Whole body, Liver, Spleen
Cerium-144	Bone
Gold-198	Lower Large Intestine
Mercury-203	Kidney
Iridium-192	Lower Large Intestine
Radon-222	Lung
Radium-226	Bone
Uranium-235	Lower Large Intestine

Some body parts have affinity for certain soluble chemical elements

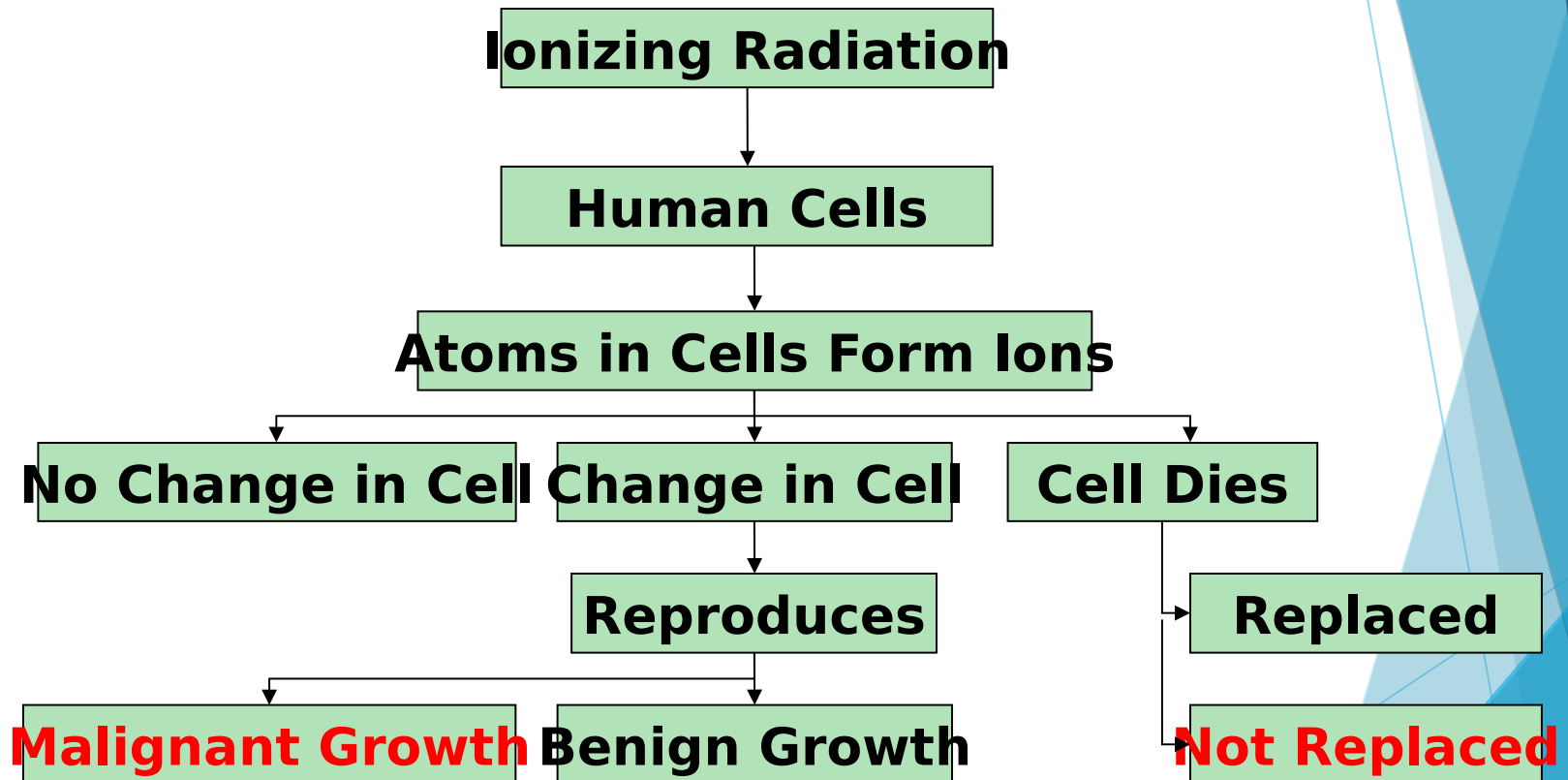
- Sr-90, Ra-226, and Pu-239 are bone-seekers, resulting in long biological half-lives
- Iodine isotopes accumulate in thyroid gland
- Cs-137 tends to accumulate in liver and spleen

Biological Effects of Ionizing Radiation

Ionizing Radiation/Cell Interactions

- ▶ Discussions of adverse biological effects generally about exposures much greater than natural background radiation
- ▶ Ionizing particles, gamma-rays, and x-rays collide with molecules in $\approx 1\%$ of 100 trillion cells that make up average human
 - Interactions generate clusters of free radicals known as reactive oxygen species (ROS) that produce random damage in cellular constituents, including DNA
 - Some types of ionizing radiation more effective generating ROS in human cells than others (e.g., α -particles 20 times more damaging than γ -rays)

Possible Outcomes of Radiation/Cell Interactions



Biological Cell Susceptibility to Radiation

- ▶ Different cells in body react differently to ionizing radiation exposure
- ▶ Cells that undergo rapid division most susceptible to radiation effects
- ▶ Hierarchy of cell susceptibility to radiation damage (highest to lowest)
 - Lymph
 - Blood
 - Reproductive and Gastrointestinal
 - Bone
 - Nerve
 - Brain
 - Muscle

Biological Effects Factors

- ▶ Potential health effects of radiation exposure depend upon
 - Dose (amount of energy deposited in body organs)
 - Ability of radiation to harm human tissue (i.e., radiation type)
 - Which organs are affected
- ▶ Most important factor is dose - amount of energy actually deposited
- ▶ Equivalent dose (Sv) used to express biological effect accounting for these factors

Types of Biological Effects

Biological effects of radiation broken into two groups according to how responses (symptoms or effects) relate to dose (amount of radiation received)

- ▶ Stochastic (probabilistic) effects
- ▶ Deterministic (dose-dependent) effects

Stochastic Effects

- ▶ Effects that have increased probability of occurrence with increasing dose; severity of effect not dose dependent
- ▶ Example: **skin cancer** and sunlight – **probability** of getting skin cancer **increases** with increasing exposure to sun
- ▶ Effects generally delayed (latent)
 - Cancer
 - Genetic changes



Deterministic Effects

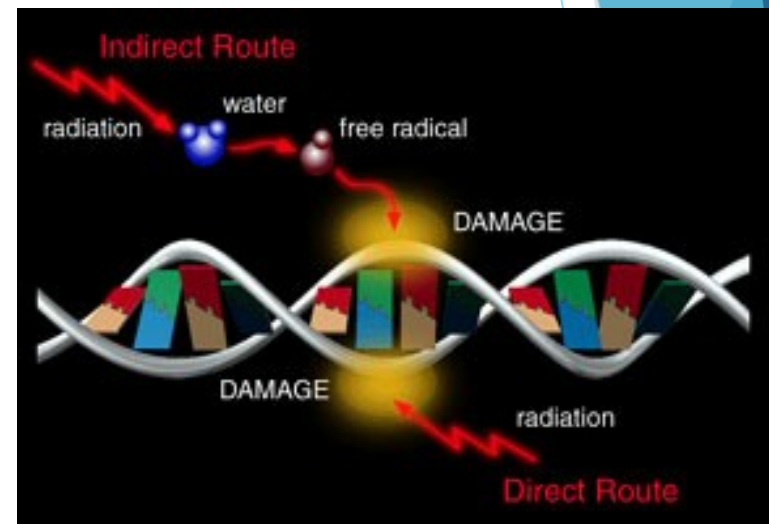
- ▶ Effects that increase in severity with increasing dose; caused by cell damage or cell death
- ▶ Example: **sunburn** and sunlight **severity** of sunburn **increases** increasing exposure to sun
- ▶ Deterministic effects have threshold above which severity increases with dose
 - Radiation-induced skin burns
 - Radiation sickness/acute radiation syndrome
 - Cataracts
 - Tumor necrosis (death)



Biological Effects of Radiation

Biological cell/tissue damage dependent upon

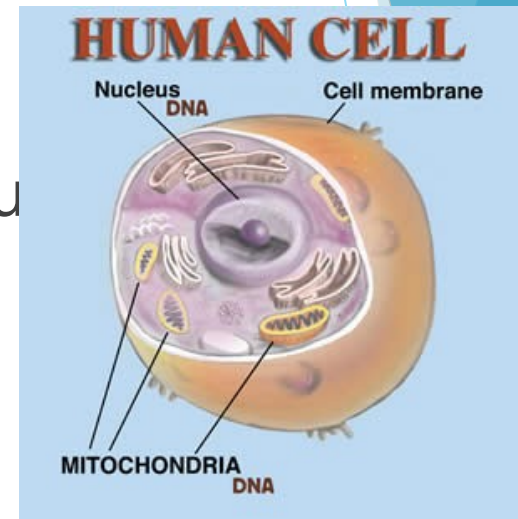
- ▶ Dose and dose rate (acute or chronic)
- ▶ Direct effects - interactions with atoms of DNA and cellular components critical to survival of cell (often result of high LET radiation)
- ▶ Indirect effects - break less critical molecules into reactive parts (primary mechanism of low LET radiation)



Biological Effects of Radiation (cont.)

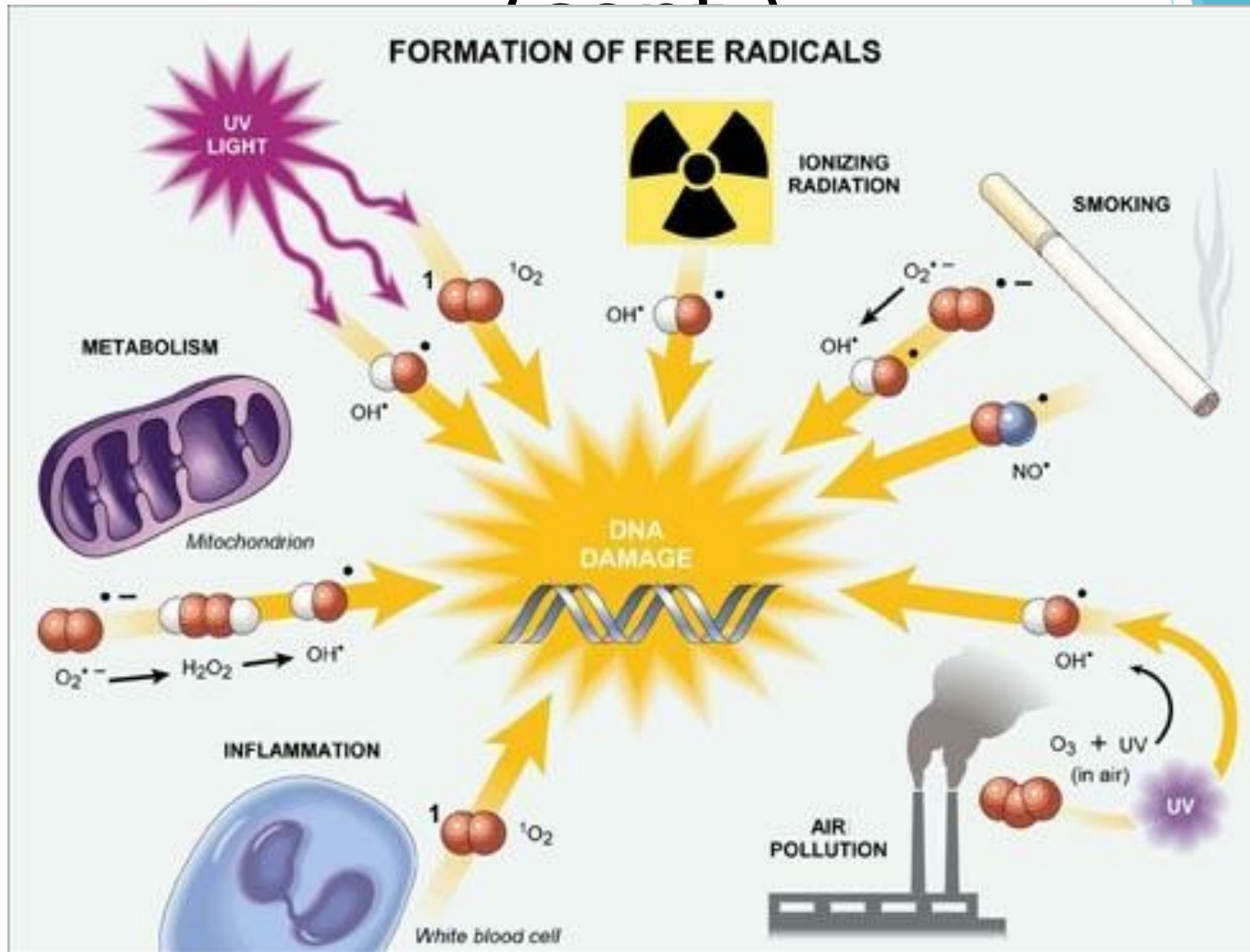
Harmful effects caused by ionization
(and excitation) in cells composing living
tissue

- ▶ Breaking of chromosomes
- ▶ Swelling of cell and cell nucleus
- ▶ Increase in cell fluid viscosity
- ▶ Increase in cell membrane permeability
- ▶ Cell destruction



Ref. *The Effects of Nuclear Weapons*, US DoD and US DOE, Third Edition, 1977,
p. 575

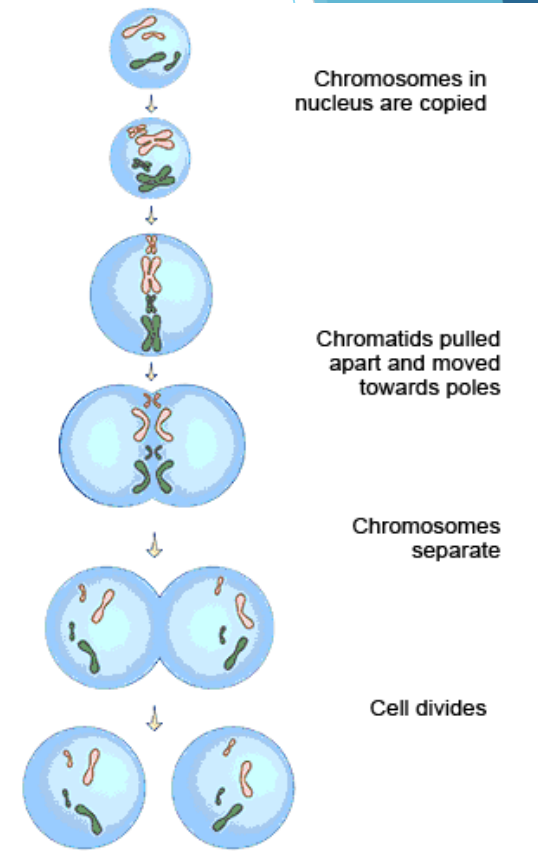
Biological Effects of Radiation



Biological Effects of Radiation (cont.)

Disruption of cell division

- ▶ Process of cell division (mitosis) may be delayed by radiation exposure so normal cell replacement inhibited
- ▶ Much cell damage of no long-term consequence as most molecules replaced regularly as part of cell lifecycle



Ref. *The Effects of Nuclear Weapons*, US DoD and US DOE, Third Edition, 1977, p. 575

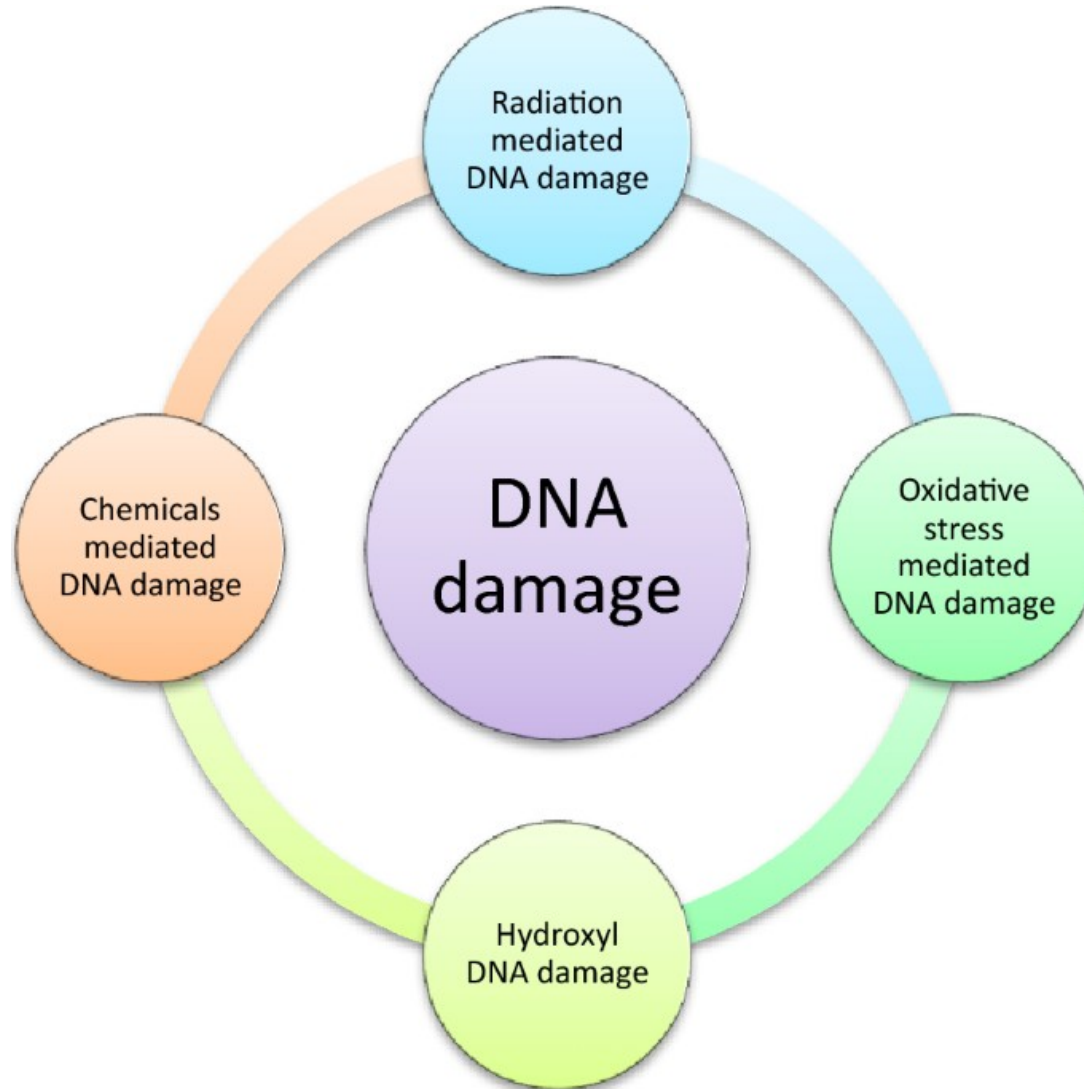
DNA Primary Focus of Radiation-Induced Damage

- ▶ Damage to DNA different than cell damage because it controls copying process
- ▶ DNA is master record for cell, coordinates its function, and itself gets copied in cell lifecycle
- ▶ Carries genetic instructions for development, functioning, growth and reproduction of all known organisms and many viruses
- ▶ Only molecule in cell that occurs in only one copy (all other molecules occur in multiple copies so damage to one or more leaves many still functional copies)

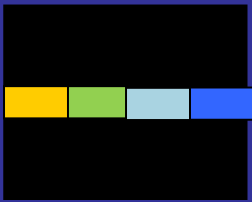
DNA Primary Focus of Radiation-Induced Damage (cont.)

- ▶ High LET radiation (α particle) generally produces DNA damage through direct effects
- ▶ Low LET radiation (β particle and gamma-ray) generally produces indirect damage through effects of free radicals and reactive oxygen species (ROS)
- ▶ Most DNA damage attributable to ionizing radiation occurs through production of ROS
- ▶ Postulated that DNA damage propagated to subsequent cell copies and passed to subsequent generations, but insufficient evidence to support hypothesis

Causes of DNA Damage

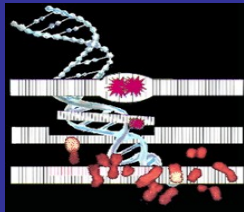


Effects of DNA Damage



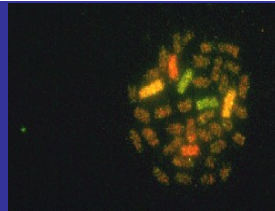
Gene Expression

A gene may respond to the radiation by changing its signal to produce protein. This may be protective or damaging.



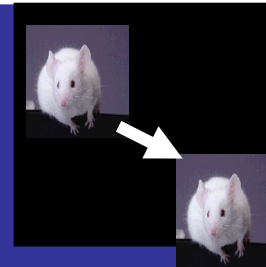
Gene Mutation

Sometimes a specific gene is changed so that it is unable to make its corresponding protein properly.



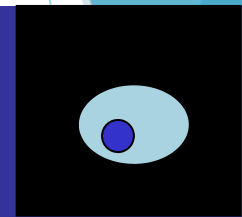
Chromosome Aberrations

Sometimes the damage affects the entire chromosome, causing it to break or recombine in an abnormal way. Sometimes parts of two different chromosomes may be combined.



Genomic Instability

Sometimes DNA damage produces later changes which may contribute to cancer.

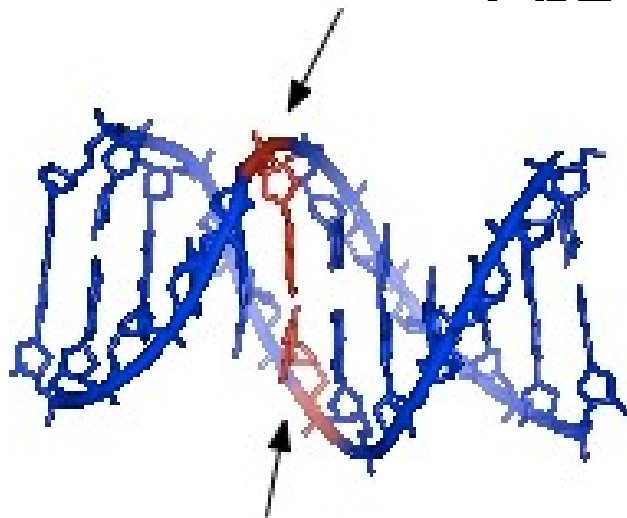


Cell Destruction

Damaged DNA may trigger apoptosis, or programmed cell death. If only a few cells are affected, this prevents reproduction of damaged DNA and protects the tissue.

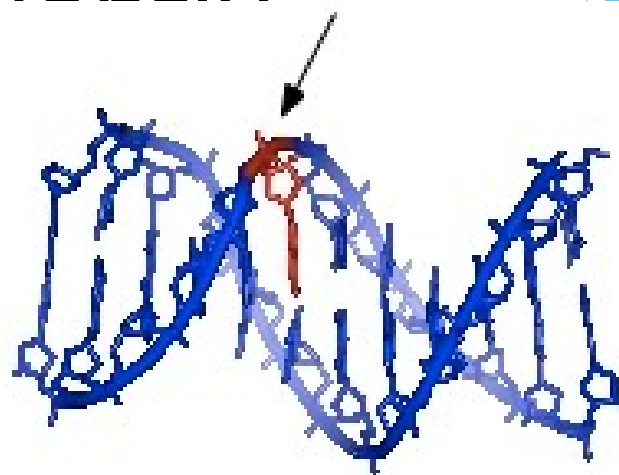
DNA Strand Breaks Occur

Frequently



Double strand breaks (DSB) occur
10 times per day per cell.

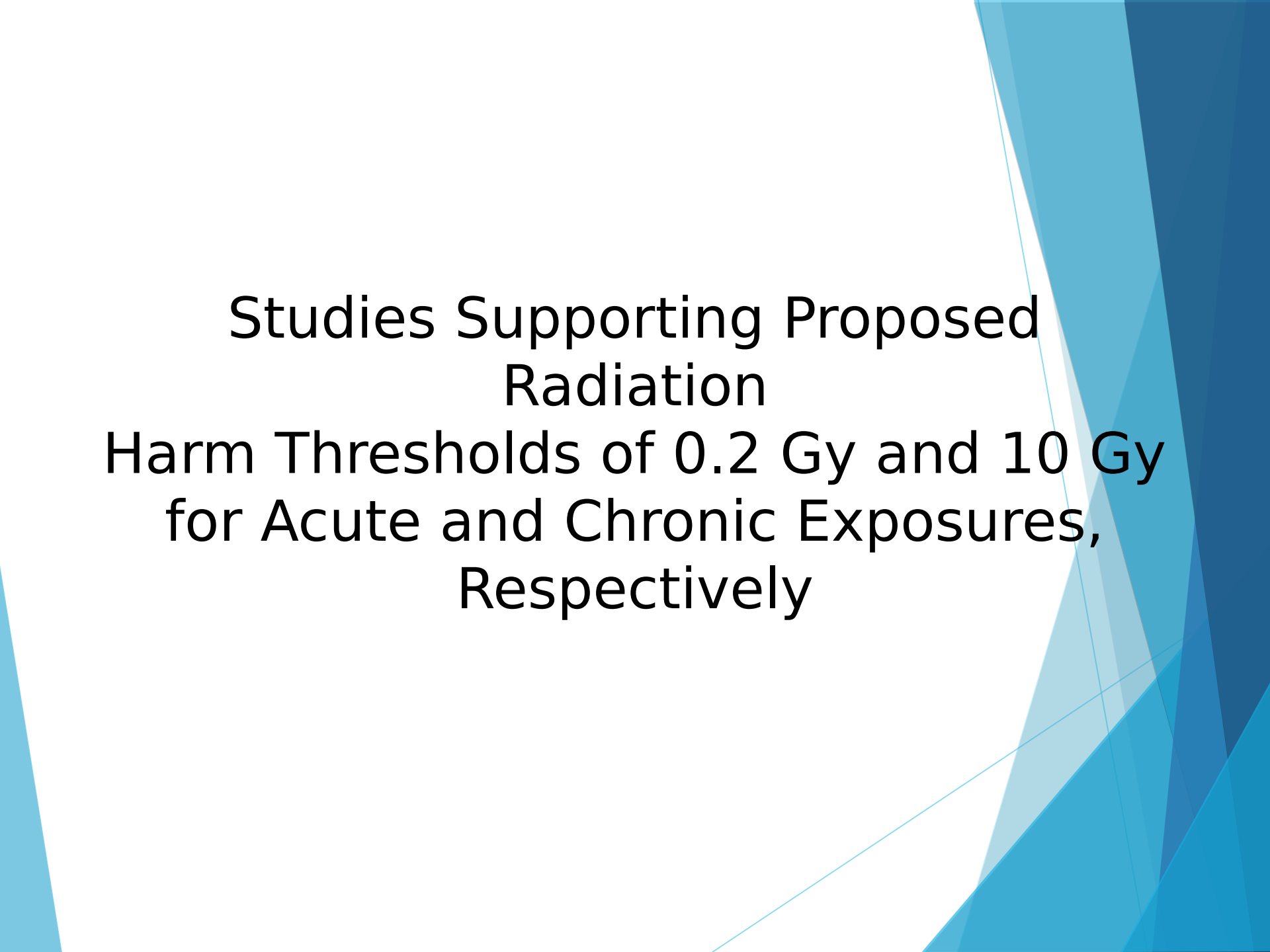
0.27 mSv/d of radiation potentially
adds 1 DSB per year.



Single strand breaks (SSB) occur
10,000 times per day per cell.

0.27 mSv/d of radiation potentially
adds 12 SSBs per day.

- Ionized oxygen molecules from metabolism principal cause of DNA breaks
- Natural background radiation (U.S. average <0.01 mSv/d) not significant contributor to DNA strand breaks

The background of the slide features abstract, overlapping geometric shapes in various shades of blue, primarily on the right side, creating a modern and professional look.

Studies Supporting Proposed Radiation Harm Thresholds of 0.2 Gy and 10 Gy for Acute and Chronic Exposures, Respectively

It's the Dose, Stupid

Paracelsus (1493-1541)

- ▶ Father of toxicology
- ▶ Established dose-response principle fundamental to toxicology
 - Amount of substance in human body dictates its effect (i.e., harmful vs beneficial)
 - It's the dose that makes the poison confirmed by presence of small amounts of toxic substances (e.g., arsenic and mercury) in human body that do not result in injury or death

High-Dose Radiation Health Effects Studies

- ▶ High-dose radiation exposures (>200 mGy) extremely uncommon
- ▶ Evidence of harm from high-dose radiation exposure almost entirely limited to
 - Radium dial painters (1915-1925)
 - Atomic bomb survivors (1945)
 - Chernobyl first responders (1986)
 - People exposed in Goiania radiological accident (1987)
- ▶ Studies provided evidence that doses <200 mGy do not increase cancer risk

Radium Dial Painters

- ▶ Ingestion of Ra-226 accumulated in bones resulting in chronic high-LET radiation exposure
- ▶ 30-year follow-up of 1155 dial painters established Ra-226 intake activity threshold of 100 μCi ($\approx 100 \mu\text{g}$ of ingested Ra-226) with associated chronic high-LET absorbed dose threshold of 10 Gy for increased cancer risk



Atomic Bomb Survivors



- ▶ Life Span Study (LSS) estimated acute plus chronic whole-body exposures
- ▶ Reconstructed dose data for $\approx 11,300$ survivors receiving high acute radiation exposures (>0.2 Gy)
- ▶ Supports proposed acute absorbed dose threshold of 0.2 Gy for increased cancer risk and shorter life expectancy

Chernobyl First Responders

- ▶ External whole-body exposures to gamma rays
- ▶ 97 first responders experienced ARS; 69 recovered
- ▶ None of 140 first responders exposed to <2 Gy died from radiation-induced causes
- ▶ Supports proposed acute absorbed dose threshold of 0.2 Gy



The Radiological Accident in Goiânia



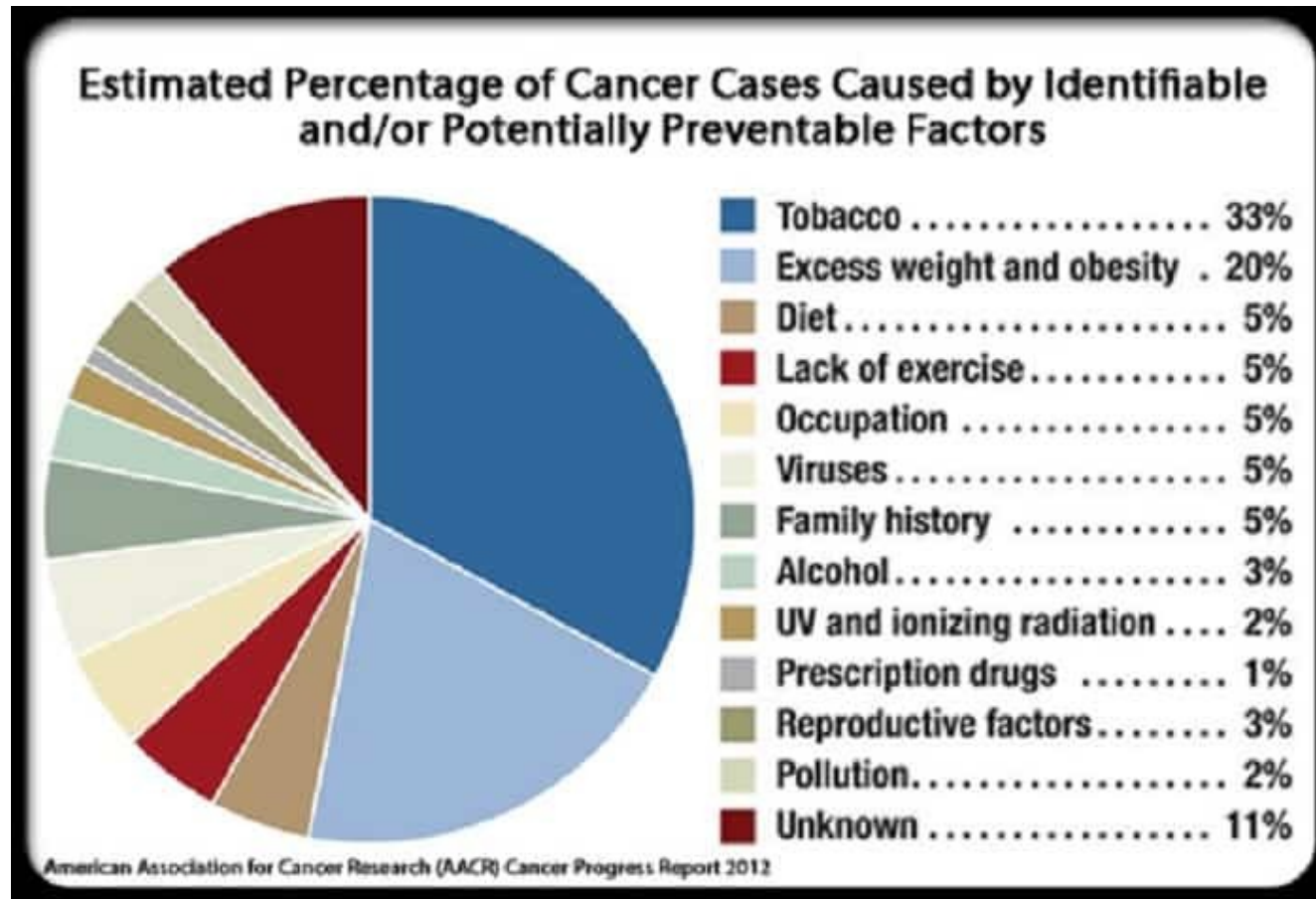
INTERNATIONAL ATOMIC ENERGY AGENCY, VIENNA, 1988

7 radiotherapy source
n from abandoned hospital
iania, Brazil, source
ule broken open, cesium
ide salt handled by many
le
asualties incurred acute
e-body external irradiation
ved by chronic whole-body
al exposure at low dose-
rate from ingested Cs-137

- ▶ 21 people with exposures >1 Gy incurred no radiation-induced cancer deaths in 25 years following accident
- ▶ Supports proposed acute absorbed dose threshold of 0.2 Gy

Radiation Exposure Effects In Three Graphics

Cancer Cause Probabilities



Ionizing
Radiation
Not a
Big
Cause of
Cancer

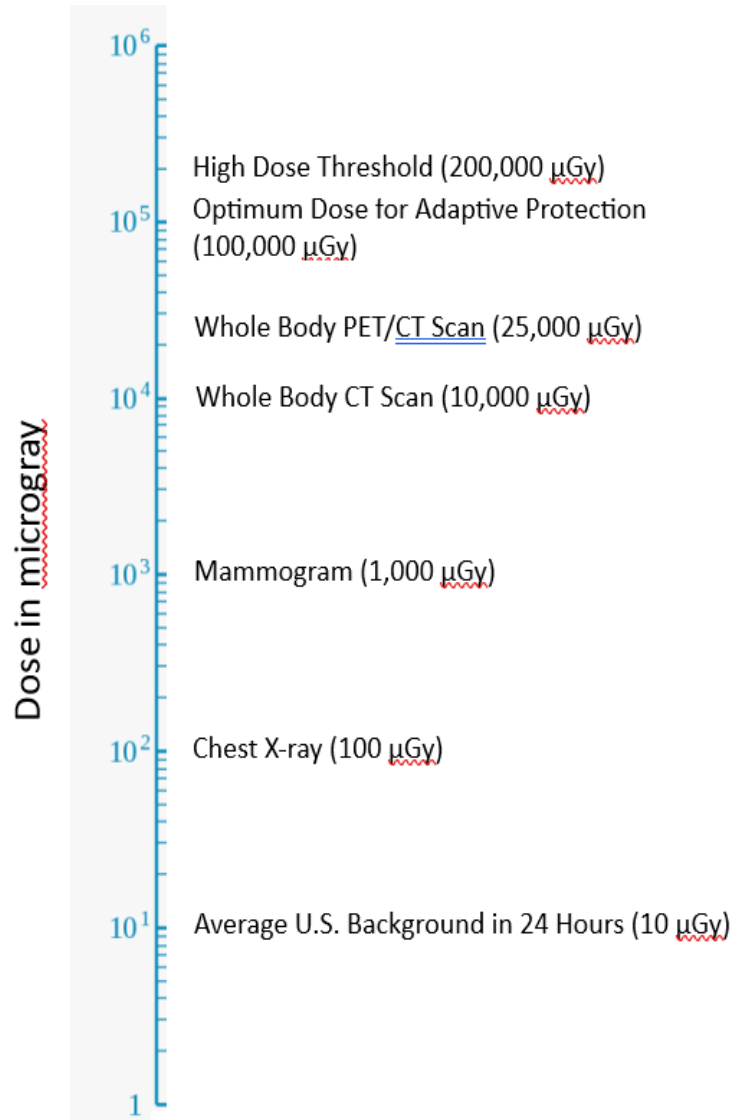


Visualizing Acute Radiation Dose Effects

Rad [Rem]	Gy [Sv]	Effect
1 000 R	10 Gy	
450 R	4.5 Gy	Lethal Dose to 50% of the Population in 30 days [LD50/30]
200 R	2 Gy 2 000 mGy	Onset of Radiation Illness
100 R	1 Gy 1 000 mGy	Observable Biological Harm
25 R	250 mGy	Typical Design-Basis Upper Target Dose
10 R	100 mGy	
1 R 1 000 mR	10 mGy	
300 mR	3 mGy 3 000 µGy	
100 mR	1 mGy 1 000 µGy	
10 mR	100 µGy	
1 mR 1 000 µR	10 µGy	
0.8 mR 800 µR	8 µGy	Day of Natural Background
100 µR	1 µGy 1 000 nGy	
0.03 mR 30 µR	300 nGy	Hour of Natural Background
10 µR	100 nGy	
1 µR 1 000 nR	10 nGy	
100 nR	1 nGy	

No adverse health effects

Acute Exposures in Perspective



Public acute (medical) exposures to low LET ionizing radiation orders of magnitude below threshold for biological harm

Low LET radiation contributes only about 4.5 μGy to natural background radiation exposure

Radiation Exposure Takeaways

- ▶ Radiation exposure does not create unique cancer risk situation; nor is such risk distinguishable from cancer risk due to other cancer-causing agents
- ▶ Public health data do not absolutely establish occurrence of cancer following acute exposure to low-dose radiation (<200 mGy)
- ▶ Studies of radiological technicians chronically exposed to low levels of radiation above normal background show no adverse biological effects
- ▶ No public health evidence for occurrence of cancer following acute or chronic exposures to low-dose radiation
- ▶ Alleged harm from low-dose radiation exposure purely speculative

Radiation Exposure Effects Summary

- Ingestion is most important route for introduction of radionuclides into organisms
- Certain body parts more specifically affected by exposure to different types of radiation sources
- Potential health effects of radiation exposure depend upon radiation type, dose,

Radiation Exposure Effects Summary (cont.)

- Effects depend upon how biological responses relate to dose
 - Stochastic effects – increasing probability of occurrence with increasing dose
 - Deterministic effects – increasing severity of response with increasing dose
- Harmful effects caused by ionization (and excitation) in cells composing living tissue

Radiation Exposure Effects Summary (cont.)

- Possible consequences of chronic exposure at rates several hundred times natural background:

- Leukopenia (low white blood cell count)
- Anemia (low red blood cell count)
- Detrimental changes in tissue structure
- Leukemia
- Malignant tumors
- Cataracts
- Increased rate of genetic mutation

Radiation Exposure Effects Summary (cont.)

- DNA is most important molecule that can be changed by radiation
- Studies have shown most radiation-induced DNA damage normally repaired by the body
- Gene mutations (unrepaired or mis-repaired DNA damage) from normal metabolism

Radiation Exposure Effects Summary (cont.)

- High radiation doses are real and serious danger
- Radiation is very good cell killer, but poor cancer producing agent
- Scientific advances say low doses of radiation produce very different biological responses than high doses
- Medical uses of radiation beneficial

Additional References

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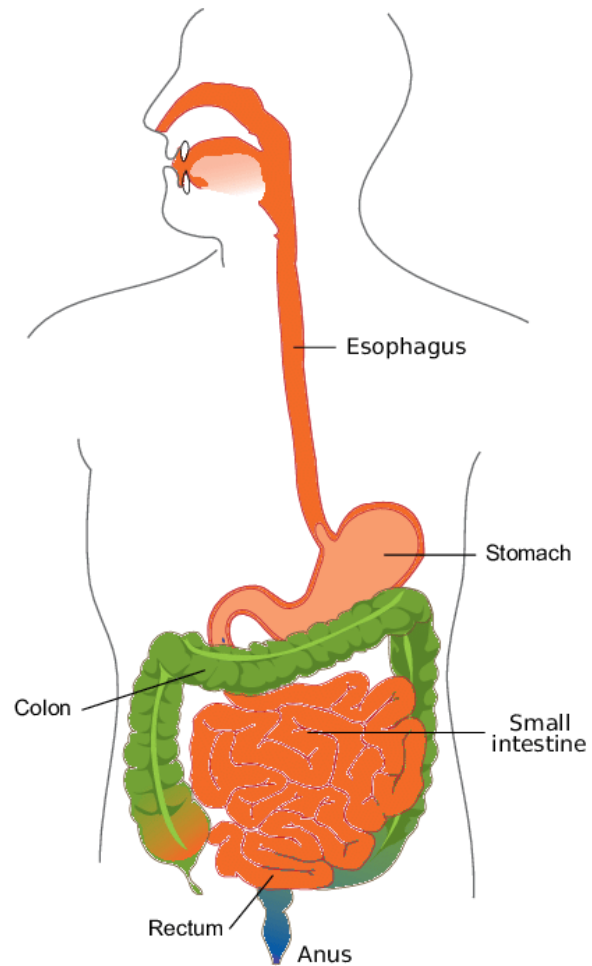
Supplemental Slides

Historical Perspective (cont.)

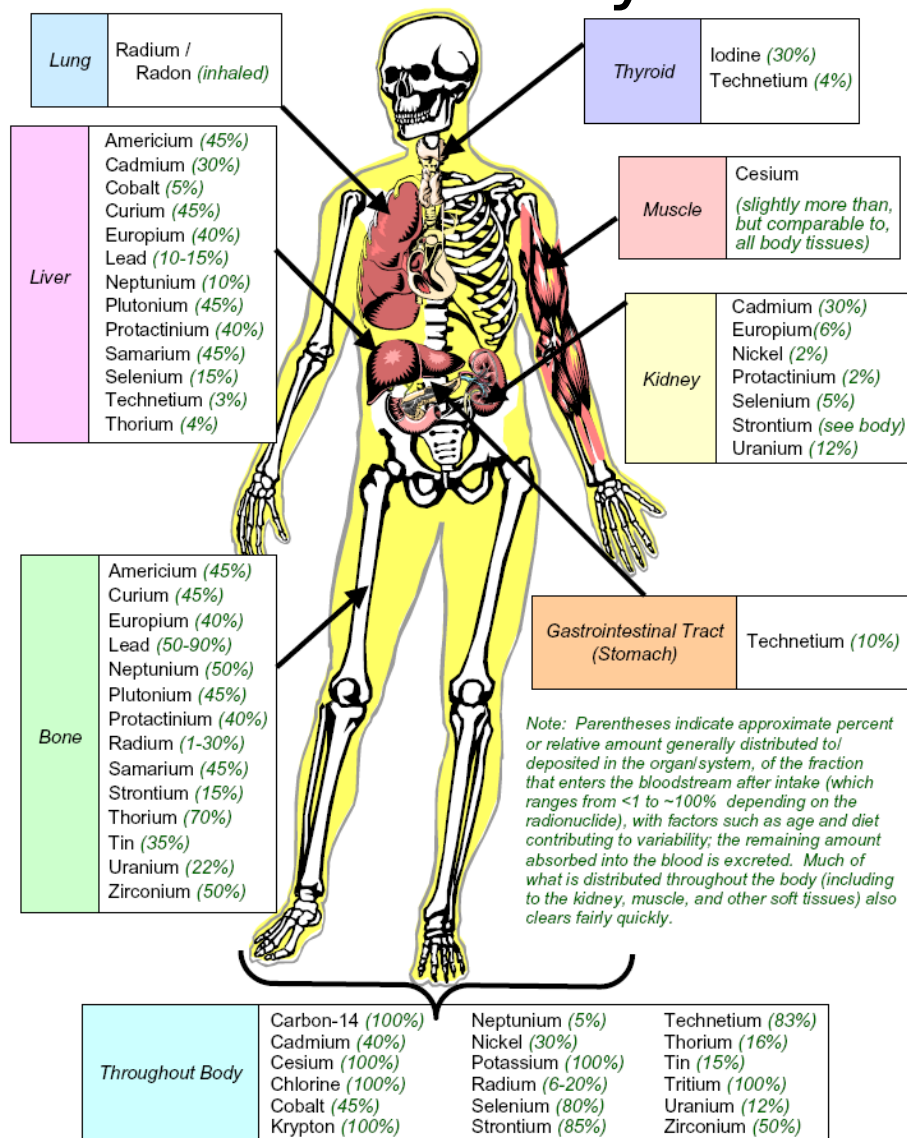
Radium poisoning case (drug overdose) occurred in 1932

- ▶ Wealthy Philadelphia industrialist and socialite Eben Byers died from self-administered massive overdose of Radithor (radium-saturated water) ingested in large quantities over three years
- ▶ Generated great publicity and created great public fear of radiation

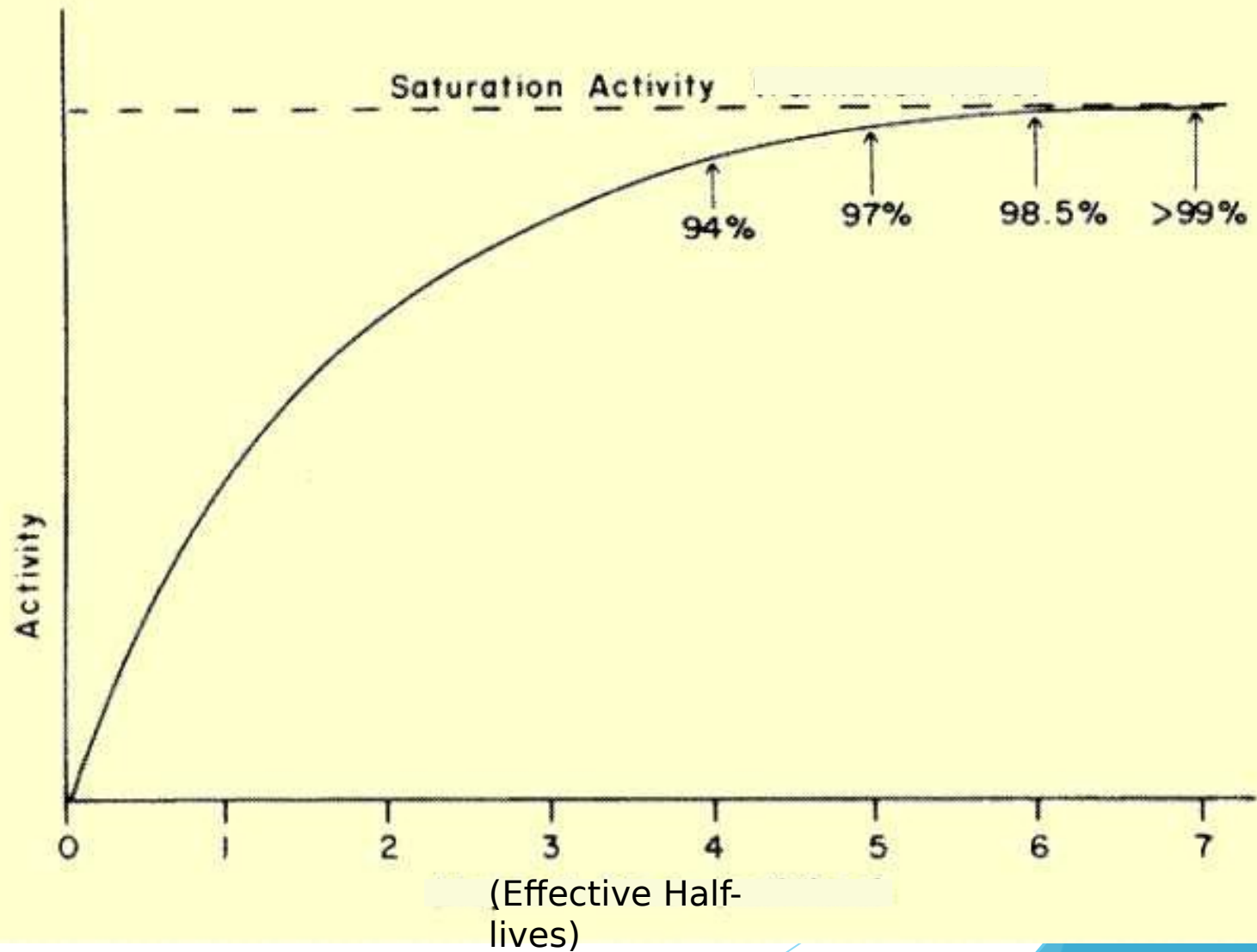
Gastrointestinal Tract



Distribution of Selected Radionuclides in Body



Radionuclide Equilibrium Activity in the Body



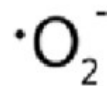
Reactive Oxygen Species (ROS)



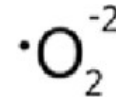
Oxygen



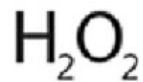
Superoxide anion



Peroxide



Hydrogen Peroxide



Hydroxyl radical



Hydroxyl ion



Biological Effects of Radiation (cont.)

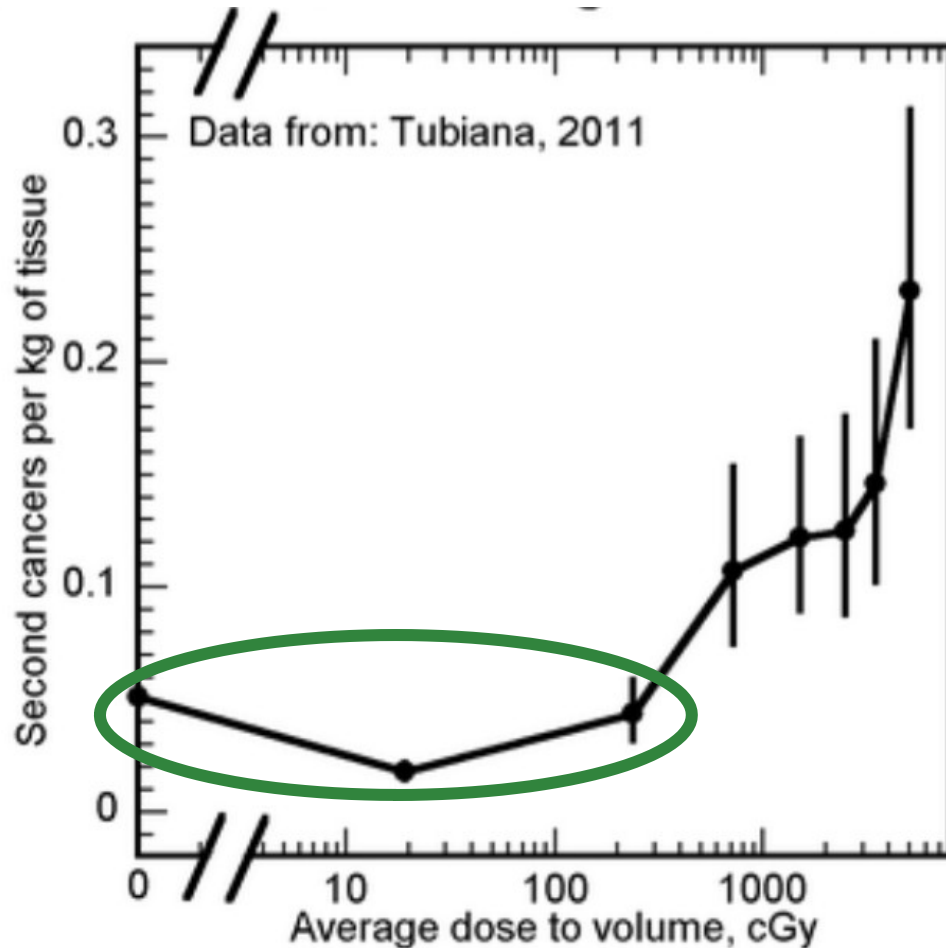
Free radicals and ROS

- ▶ Highly reactive chemical molecules
 - Free radical is molecular species with unpaired electron
 - ROS is subset of free radicals containing oxygen atoms
- ▶ Byproducts of normal body metabolism; intrinsic to cellular functioning
- ▶ Also generated by external mechanisms
 - Ionizing radiation not even most prominent external mechanism
- ▶ Harmful free radicals neutralized by antioxidants

DNA Repair

- ▶ Double-helical structure of DNA ideally suited for repair because it carries two separate copies of all genetic information—one in each of two strands
- ▶ Each human cell contains multiple DNA repair systems, each with its own enzymes and preferences for type of damage recognized
- ▶ Most systems use the undamaged strand of double helix as template to repair damaged strand

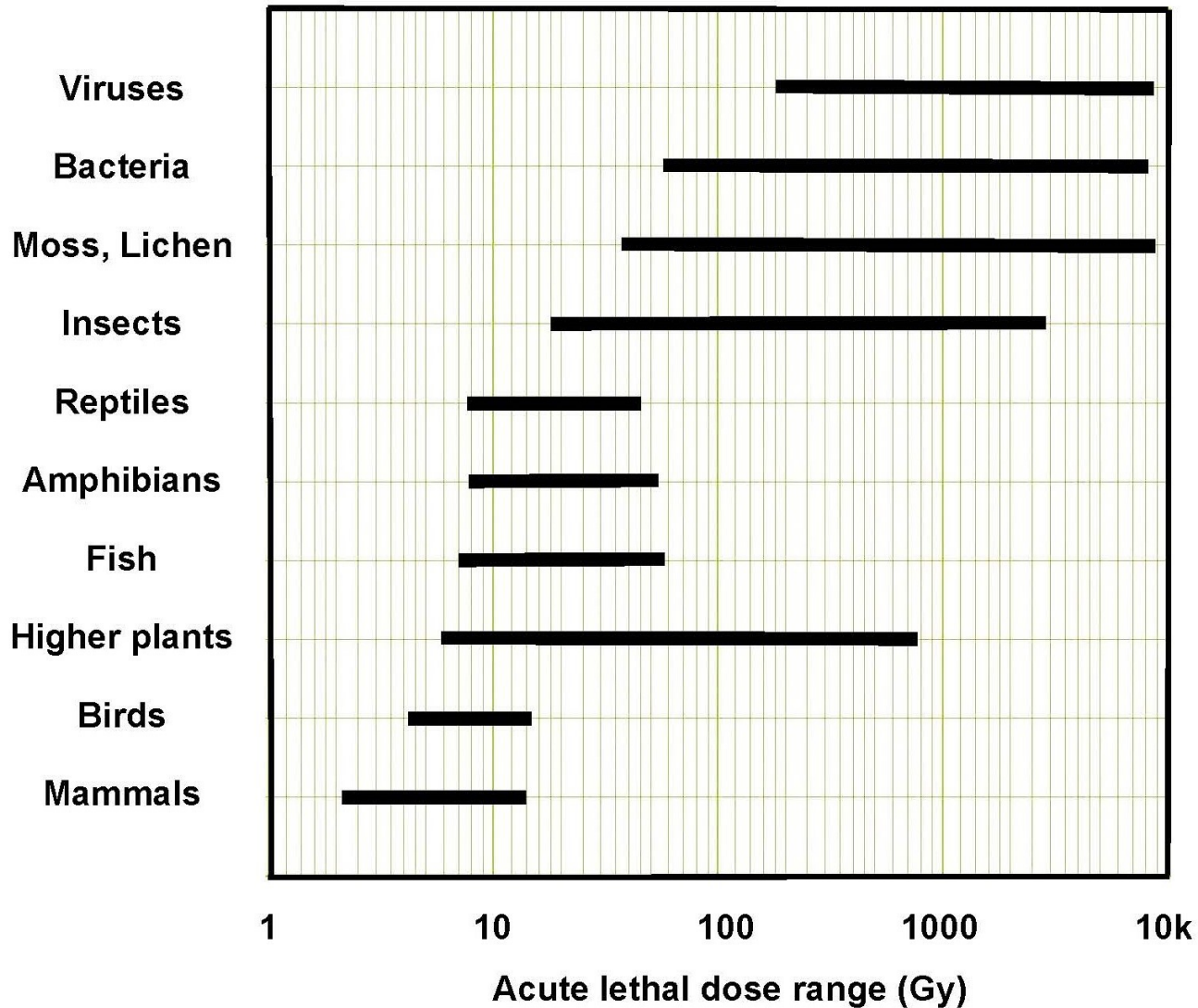
Secondary Cancers *Reduced*



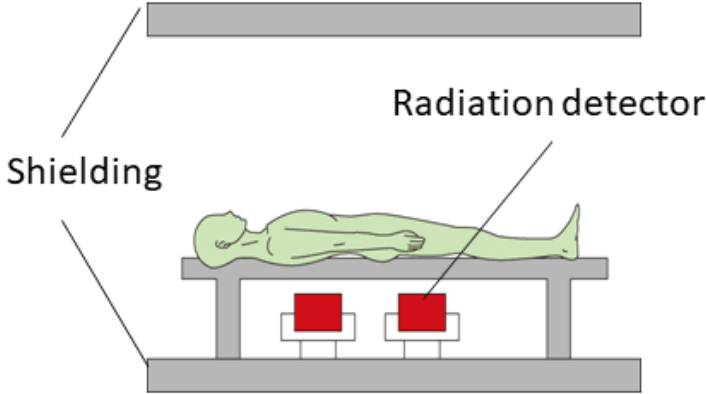
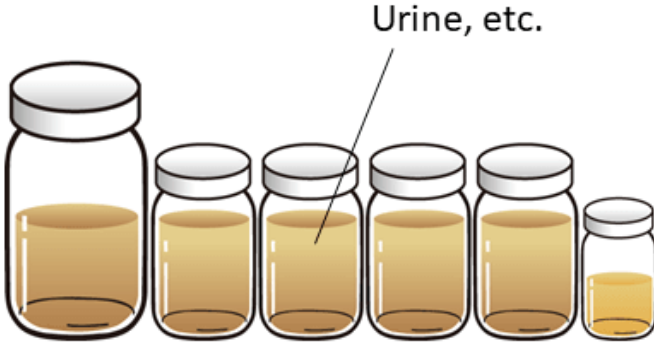
Regions

Reduction of secondary cancers per kg of tissue in regions of body subjected to radiation dose of ~200 cGy during radiation therapy, in comparison to regions not subjected to any radiation dose

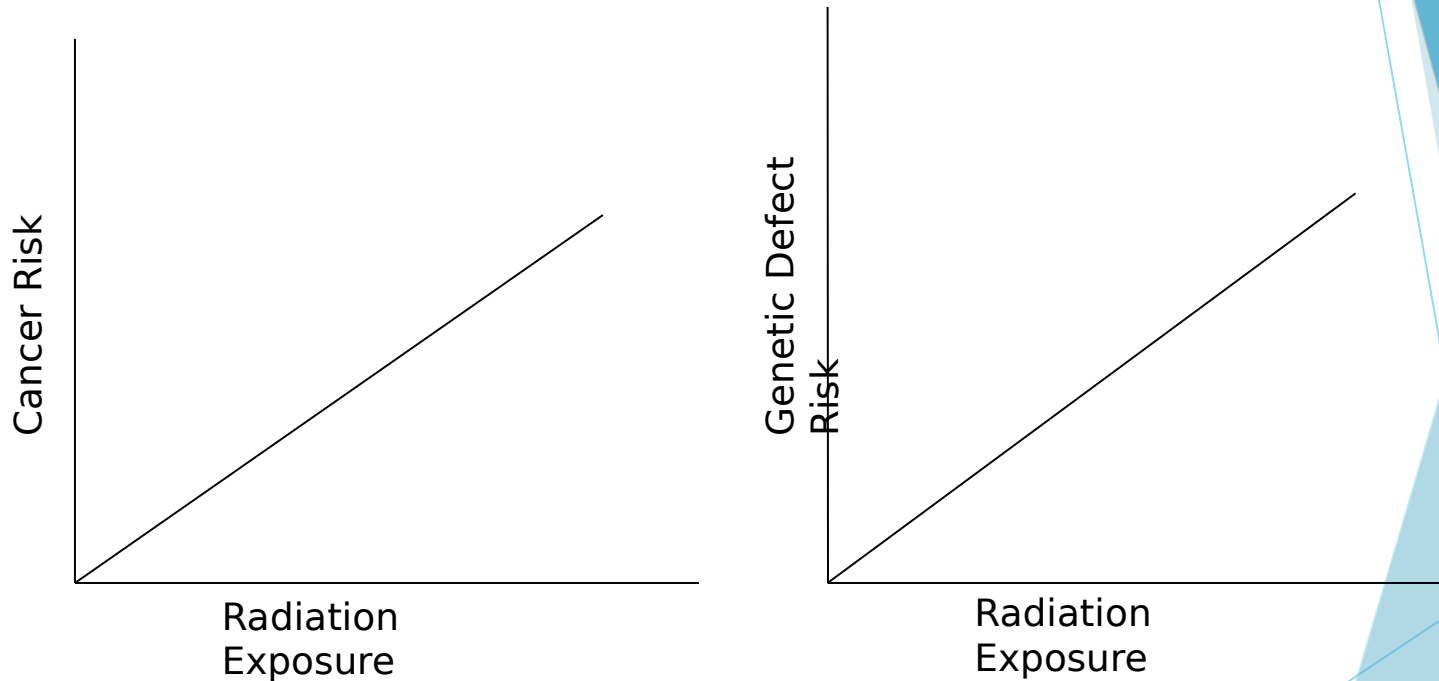
Organism Acute Lethal Radiation Dose Ranges



Comparison of Methods of Assessing Internal Radioactivity

Direct counting	Bioassay
Directly measure the human body	Indirect measurement
Need to spare time to receive direct measurements	Submit samples (urine, feces, etc.)
Mainly target materials that emit γ -rays	Able to measure all radioactive materials
Short measuring time using the apparatus	Chemical analysis takes time.
Accurate dose assessment	Large margin of error in results of dose assessment
 The diagram illustrates the direct counting method. A human figure is lying on a table. Below the table, two red rectangular units represent radiation detectors. A line labeled 'Shielding' points to a thick grey horizontal bar positioned above the detectors. Another line labeled 'Radiation detector' points to one of the red units. The entire setup is on a grey base.	 The diagram illustrates the bioassay method. It shows a row of six glass vials containing a yellow liquid. A line labeled 'Urine, etc.' points to the third vial from the left. The vials are of varying heights and are arranged on a white surface.

Linear No-threshold (LNT) Dose-Response Model



Extrapolation is from effects of very high (acute) doses received by atomic bomb survivors.